# EAST Search History

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|---|---|---|---|---|---|---|
| L2 | 5923 | hepatocyte adj growth adj factor | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 15:08 |
| L3 | 7664 | L2 or HGF | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 15:09 |
| L4 | 279769 | antibody or immunoglobulin | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 15:09 |
| L5 | 6083 | L4 and L3 | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 15:10 |
| L6 | 3862 | neutral$5 and L5 | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 15:22 |
| L7 | 448 | H61 | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 15:22 |
| L8 | 177 | H68 | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 15:22 |
| L9 | 41 | L7 and L8 | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 15:29 |

# EAST Search History

| | | | | | | |
|---|---|---|---|---|---|---|
| L10 | 1 | L6 and L9 | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 15:23 |
| L11 | 584 | L7 or L8 | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 15:30 |
| L12 | 11 | L11 and L6 | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 18:03 |
| L13 | 62441 | chung.in. | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 18:04 |
| L14 | 27 | L13 and L2 | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 18:05 |
| L15 | 60 | L13 and L3 | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 18:09 |
| L16 | 3 | Hur.in. and L3 | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/05/21 18:09 |

FILE COVERS 1907 - 22 May 2007 VOL 146 ISS 22
FILE LAST UPDATED: 21 May 2007 (20070521/ED)



```
=> s hepatocyte (s) growth (s) factor
         48807 HEPATOCYTE
         43922 HEPATOCYTES
         63555 HEPATOCYTE
                 (HEPATOCYTE OR HEPATOCYTES)
       1347081 GROWTH
          4495 GROWTHS
       1349368 GROWTH
                 (GROWTH OR GROWTHS)
       1039109 FACTOR
        939318 FACTORS
       1637928 FACTOR
                 (FACTOR OR FACTORS)
L1        8771 HEPATOCYTE (S) GROWTH (S) FACTOR

=> s HGF
          5273 HGF
           202 HGFS
L2        5375 HGF
                 (HGF OR HGFS)

=> s L1 or L2
L3        9819 L1 OR L2

=> s neutral? (s) epitope
        512504 NEUTRAL?
         40689 EPITOPE
         42171 EPITOPES
         61620 EPITOPE
                 (EPITOPE OR EPITOPES)
L4        3106 NEUTRAL? (S) EPITOPE
```

=> s L3 and L4
L5 4 L3 AND L4

=> d ibib abs

L5 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:104586 CAPLUS
DOCUMENT NUMBER: 146:309794
TITLE: A **neutralizable epitope** is induced on **HGF** upon its interaction with its receptor cMet
AUTHOR(S): Kim, Kisu; Hur, Youngmi; Ryu, En-Kyung; Rhim, Jung-Hyo; Choi, Cha Yong; Baek, Cheol-Min; Lee, Jae-Ho; Chung, Junho
CORPORATE SOURCE: Cancer Research Institute, Seoul National University College of Medicine, Seoul, S. Korea
SOURCE: Biochemical and Biophysical Research Communications (2007), 354(1), 115-121 CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new conformational **neutralizable epitope** is created on **hepatocyte growth factor (HGF)**, when it interacts with its receptor, cMet. By immunizing rabbits with **HGF**-cMet complex, we successfully generated a monoclonal antibody (SFN68) that inhibits **HGF**-cMet interaction, and blocks the biol. function mediated by **HGF**. To define the epitope, we screened out an epitope-mimicking peptide, KSLSRHDHIHHH, from a phage display of combinatorial peptide library. In mol. mimicry this peptide bound to cMet and inhibited **HGF**-cMet interaction. No humoral response was induced to this epitope-mimicking peptide when immunization was done with **HGF** alone.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 2-4 ibib abs

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:94360 CAPLUS
DOCUMENT NUMBER: 144:169296

TITLE: Fully Human Monoclonal Antibodies to **Hepatocyte Growth Factor** with Therapeutic Potential against **Hepatocyte Growth Factor**/c-Met-Dependent Human Tumors

AUTHOR(S): Burgess, Teresa; Coxon, Angela; Meyer, Susanne; Sun, Jan; Rex, Karen; Tsuruda, Trace; Chen, Qing; Ho, Shu-Yin; Li, Luke; Kaufman, Stephen; McDorman, Kevin; Cattley, Russell C.; Sun, Jilin; Elliott, Gary; Zhang, Ke; Feng, Xiao; Jia, Xiao-Chi; Green, Larry; Radinsky, Robert; Kendall, Richard

CORPORATE SOURCE: Department of Oncology Research, Amgen, Inc., Thousand Oaks, CA, USA

SOURCE: Cancer Research (2006), 66(3), 1721-1729
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB C-Met is a well-characterized receptor tyrosine kinase for **hepatocyte growth factor** (**HGF**). Compelling evidence from studies in human tumors and both cellular and animal tumor models indicates that signaling through the **HGF**/c-Met pathway mediates a plethora of normal cellular activities, including proliferation, survival, migration, and invasion, that are at the root of cancer cell dysregulation, tumorigenesis, and tumor metastasis. Inhibiting **HGF**-mediated signaling may provide a novel therapeutic approach for treating patients with a broad spectrum of human tumors. Toward this goal, we generated and characterized five different fully human monoclonal antibodies that bound to and neutralized human **HGF**. Antibodies with subnanomolar affinities for **HGF** blocked binding of human **HGF** to c-Met and inhibited **HGF**-mediated c-Met phosphorylation, cell proliferation, survival, and invasion. Using a series of human-mouse chimeric **HGF** proteins, we showed that the **neutralizing** antibodies bind to a unique **epitope** in the ζ-chain of human **HGF**. Importantly, these antibodies inhibited **HGF**-dependent autocrine-driven tumor growth and caused significant regression of established U-87 MG tumor xenografts. Treatment with anti-**HGF** antibody rapidly inhibited tumor cell proliferation and significantly

increased the proportion of apoptotic U-87 MG tumor cells in vivo. These
results suggest that an antibody to an epitope in the {szligbeta}-chain of
**HGF** has potential as a novel therapeutic agent for treating patients with **HGF**-dependent tumors.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:429434 CAPLUS
DOCUMENT NUMBER: 142:480775
TITLE: Neutralizing antibody to **hepatocyte growth factor**
INVENTOR(S): Chung, Junho; Hur, Youngmi
PATENT ASSIGNEE(S): National Cancer Center, S. Korea
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005044848 | A1 | 20050519 | WO 2004-KR2888 | 20041109 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO,
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,

NE, SN, TD, TG
KR 2005045419 A 20050517 KR 2003-79482
20031111
AU 2004287743 A1 20050519 AU 2004-287743
20041109
EP 1694700 A1 20060830 EP 2004-800068
20041109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT,
IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS
CN 1878790 A 20061213 CN 2004-80033164
20041109
US 2007036789 A1 20070215 US 2006-578836
20060510
IN 2006DN03385 A 20070504 IN 2006-DN3385
20060612
PRIORITY APPLN. INFO.: KR 2003-79482 A
20031111
WO 2004-KR2888 W
20041109
AB The authors disclose the preparation and characterization of
neutralizing
antibodies against human **hepatocyte growth
factor** (**HGF**). The antibodies are capable of preventing
**HGF** binding to its receptor and may find utility in treating
intractable diseases and cancers.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE
FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:471599 CAPLUS
DOCUMENT NUMBER: 135:194201
TITLE: Neutralizing monoclonal antibodies to
**hepatocyte growth factor**
/scatter **factor** (**HGF**/SF) display
antitumor activity in animal models
AUTHOR(S): Cao, Brian; Oskarsson, Marianne; Zhao, Ping;
Kort,
Eric J.; Fisher, Robert J.; Wang, Ling-Mei;
Vande
Woude, George F.
CORPORATE SOURCE: Van Andel Research Institute, Grand Rapids,
MI, 49503,
USA
SOURCE: Proceedings of the National Academy of
Sciences of the
United States of America (2001), 98(13),
7443-7448
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **hepatocyte growth factor** (**HGF**/SF) receptor, Met, regulates mitogenesis, motility, and morphogenesis in a cell type-dependent fashion. Activation of Met via autocrine, paracrine, or mutational mechanisms can lead to tumorigenesis and metastasis and numerous studies have linked inappropriate expression of this ligand-receptor pair to most types of human solid tumors. To prepare mAbs to human **HGF**/SF, mice were immunized with native and denatured prepns. of the ligand. Recloned mAbs were tested in vitro for blocking activity against scattering and branching morphogenesis. Our results show that no single mAb was capable of **neutralizing** the in vitro activity of **HGF**/SF, and that the ligand possesses a min. of three **epitopes** that must be blocked to prevent Met tyrosine kinase activation. In vivo, the neutralizing mAb combination inhibited s.c. growth in athymic nu/nu mice of tumors dependent on an autocrine Met-**HGF**/SF loop. Importantly, growth of human glioblastoma multiforme xenografts expressing Met and **HGF**/SF were markedly reduced in the presence of **HGF**/SF-neutralizing mAbs. These results suggest interrupting autocrine and/or paracrine Met-**HGF**/SF signaling in tumors dependent on this pathway is a possible intervention strategy.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s chung J?/au
L6 3733 CHUNG J?/AU

=> s hur Y?/au
L7 112 HUR Y?/AU

=> s L6 or L7
L8 3840 L6 OR L7

=> s L8 and L3
L9 5 L8 AND L3

=> d 1-5 ibib abs

L9 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:104586 CAPLUS
DOCUMENT NUMBER: 146:309794
TITLE: A neutralizable epitope is induced on **HGF** upon its interaction with its receptor cMet
AUTHOR(S): Kim, Kisu; **Hur, Youngmi**; Ryu, En-Kyung; Rhim, Jung-Hyo; Choi, Cha Yong; Baek, Cheol-Min; Lee, Jae-Ho; **Chung, Junho**
CORPORATE SOURCE: Cancer Research Institute, Seoul National University College of Medicine, Seoul, S. Korea
SOURCE: Biochemical and Biophysical Research Communications (2007), 354(1), 115-121 CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new conformational neutralizable epitope is created on **hepatocyte growth factor** (**HGF**), when it interacts with its receptor, cMet. By immunizing rabbits with **HGF**-cMet complex, we successfully generated a monoclonal antibody (SFN68) that inhibits **HGF**-cMet interaction, and blocks the biol. function mediated by **HGF**. To define the epitope, we screened out an epitope-mimicking peptide, KSLSRHDHIHHH, from a phage display of combinatorial peptide library. In mol. mimicry this peptide bound to cMet and inhibited **HGF**-cMet interaction. No humoral response was induced to this epitope-mimicking peptide when immunization was done with **HGF** alone.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:379725 CAPLUS
DOCUMENT NUMBER: 145:26137
TITLE: Functional expression of single-chain variable fragment antibody against c-Met in the cytoplasm of Escherichia coli
AUTHOR(S): Heo, Mi-Ae; Kim, Su-Hyun; Kim, So-Yeon; Kim, Yu-Jin; **Chung, Junho**; Oh, Min-Kyu; Lee, Sun-Gu
CORPORATE SOURCE: Department of Chemical and Biochemical Engineering,

Pusan National University, Pusan, 609-735, S. Korea
SOURCE: Protein Expression and Purification (2006), 47(1), 203-209
CODEN: PEXPEJ; ISSN: 1046-5928
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB C-Met, a high affinity receptor for **hepatocyte growth factor**/scatter **factor**, shown to be overexpressed in a variety of malignant cells, is a potential biomarker as well as a therapeutic target. Thus, single-chain antibody fragment (scFv) specific for c-Met is expected to be efficiently employed in the clin. treatment or imaging of many cancer cells. Here, the authors constructed the expression system for anti-c-Met scFv fused with T7 tag at its N-terminus using pET vector and investigated the expression conditions to achieve a functional and soluble expression of the scFv in the cytoplasm of recombinant Escherichia coli. The redox potential of E. coli cytoplasm was the most critical factor for the functional expression of anti-c-Met scFv. The employment of a host with oxidizing cytoplasm, E. coli trxB/gor double mutant, improved the productivity of functional anti-c-Met scFv by approx. 10-fold compared to the production of anti-c-Met scFv in the reducing cytoplasm of wild type E. coli. Productivity of functional anti-c-Met scFv could be further enhanced by co-expressing mol. chaperones such as GroELS, trigger factor, and DsbC with the scFv. Coexpression of DsbC increased the yield of functional anti-c-Met scFv about 2.5-fold in the cytoplasm of E. coli trxB/gor mutant compared to the production of scFv without DsbC coexpression. Lowering the IPTG concentration from 1 to 0.05 mM led to the slight enhancement, approx. 1.6-fold, of productivity of functional scFv. Although the use of low temperature for anti-c-Met scFv expression increased the ratio of soluble scFv fraction to insol. fraction, productivity

of soluble scFv decreased owing to the significant reduction of expression rate.
The addition of 0.5 M sucrose in the medium inhibited the formation of
intracellular insol. anti-c-Met scFv. To purify the anti-c-Met scFv
simply, the authors fused hexahistidine at the C-terminus of scFv and
purified the scFv showing 98% of purity through the interaction between
Ni2+ and histidine.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1278399 CAPLUS
DOCUMENT NUMBER: 144:49795
TITLE: Generation of a rabbit VH domain antibody polyspecific
to c-Met and adenoviral knob protein
AUTHOR(S): Im, Shin-Young; Kim, Ki Su; Yun, Chae-Ok; Kim,
Joo-Hang; Yi, Kye-Sook; **Chung, Junho**
CORPORATE SOURCE: Cancer Research Institute, Seoul National University
College of Medicine, Seoul, S. Korea
SOURCE: Biochemical and Biophysical Research Communications
(2006), 339(1), 305-312
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several types of bispecific antibodies with affinity to both adenoviral
coat proteins and a targeted antigen have been developed with the aim of
providing the specific delivery of adenoviral gene therapy vehicle. From
a phage display library of combinatorial dAb2s (each with an
anti-adenoviral knob protein VH fragment linked with an anti-c-Met VH),
the authors serendipitously enriched and isolated a clone, JS5, that has
polyspecificity such that it binds both the adenoviral knob protein and
c-Met, despite having only one VH domain. The authors' indirect
observations suggest that the polyspecificity of JS5 is developed through

accumulation of antibody specificity. The method of sequential immunization of a rabbit, first with the adenoviral knob protein and then with target antigens, may provide a method by which monoclonal antibodies with stand-alone polyspecificity may be developed. Such targeted polyspecific antibodies could readily be used for re-directing adenoviral vectors to target cells.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:429434 CAPLUS
DOCUMENT NUMBER: 142:480775
TITLE: Neutralizing antibody to **hepatocyte growth factor**
INVENTOR(S): **Chung, Junho; Hur, Youngmi**
PATENT ASSIGNEE(S): National Cancer Center, S. Korea
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005044848 | A1 | 20050519 | WO 2004-KR2888 | 20041109 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,

SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG
KR 2005045419 A 20050517 KR 2003-79482 20031111
AU 2004287743 A1 20050519 AU 2004-287743 20041109
EP 1694700 A1 20060830 EP 2004-800068 20041109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS
CN 1878790 A 20061213 CN 2004-80033164 20041109
US 2007036789 A1 20070215 US 2006-578836 20060510
IN 2006DN03385 A 20070504 IN 2006-DN3385 20060612
PRIORITY APPLN. INFO.: KR 2003-79482 A 20031111
WO 2004-KR2888 W 20041109
AB The authors disclose the preparation and characterization of neutralizing antibodies against human **hepatocyte growth factor** (**HGF**). The antibodies are capable of preventing **HGF** binding to its receptor and may find utility in treating intractable diseases and cancers.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:604215 CAPLUS
DOCUMENT NUMBER: 141:154893
TITLE: The Met receptor and α6β4 integrin can function independently to promote carcinoma invasion
AUTHOR(S): **Chung, Jun**; Yoon, Sang-Oh; Lipscomb, Elizabeth A.; Mercurio, Arthur M.
CORPORATE SOURCE: Beth Israel Deaconess Medical Center, Division of Cancer Biology and Angiogenesis, Department of Pathology, Harvard Medical School, Boston, MA, 02215, USA
SOURCE: Journal of Biological Chemistry (2004), 279(31), 32287-32293

CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It has been proposed that a constitutive, phys. association of the Met receptor and the α6β4 integrin exists on the surface of invasive carcinoma cells and that **hepatocyte growth factor** (**HGF**)-mediated invasion is dependent on α6β4. The potential significance of these results prompted us to re-examine this hypothesis. Using three different carcinoma cell lines that express both Met and α6β4, we were unable to detect the constitutive association of these receptors by co-immunopptn. Moreover, carcinoma cells that lacked expression of α6β4 exhibited Met-dependent invasion toward **HGF**, and increasing Met expression by viral infection of these cells enhanced invasion without inducing α6β4 expression. Although expression of α6β4 in such cells enhanced their invasion to **HGF**, it also enhanced their ability to invade toward other chemoattractants such as lysophosphatidic acid, and this latter invasion was not inhibited by a function-blocking Met antibody. Finally, depletion of β4 by RNA interference in invasive carcinoma cells that express both receptors reduced the ability of these cells to invade toward **HGF** by .apprx.25%, but it did not abrogate their invasion. These data argue that the invasive function of Met can be independent of α6β4 and that α6β4 has a generic influence on the invasion of carcinoma cells that is not specific to Met.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT